In The Claims

Please cancel claims 1-15, without prejudice.

Please add the following new claims:

--16. (New) A method for identifying a molecule which modulates the interaction between at least a first and second protein, comprising:

measuring the interaction of a first hybrid protein and a second hybrid protein in the presence of a test molecule, wherein the first hybrid protein comprises a first domain and the first protein and the second hybrid protein comprises a second domain and the second protein, wherein interaction of the first protein and the second protein causes a detectable response; and

comparing the detectable response in the presence and absence of the test molecule, wherein a difference between the responses is indicative of a test molecule that modulates protein-protein interaction.

17. (New) The method of claim 16, wherein the first domain is a DNA-binding moiety and the second domain is a transcriptional activation or a transcriptional repressor moiety and the detectable response is the expression of a detectable gene.

18. (New) The method of claim 17, wherein the DNA-binding moiety and the transcriptional activation moiety are derived from a single transcriptional activator.

19. (New) The method of claim 17, wherein the DNA-binding moiety and the transcriptional activation moiety are derived from a different proteins.

20. (New) The method of claim 17, wherein the detectable gene encodes a protein selected

21. (New) The method of claim 16, wherein the test molecule is a protein or bioactive molecule.

22. (New) The method of claim 17, wherein the detectable gene is present in a host cell.

23. (New) The method of claim 22, wherein the host cell further comprises a first recombinant gene encoding the first hybrid protein, a second recombinant gene encoding the second hybrid protein, or a third recombinant gene encoding the test molecule.

24. (New) The method of claim 23, wherein the host cell contains both the first gene and the second gene.

25. (New) The method of claim 23, wherein the host cell contains the first, second and third gene.

26. (New) The method of claim 25, wherein the host cell is cultured under conditions that allows for expression of the genes.

27. (New) The method of claim 16, wherein the test molecules is derived from an environmental library.

28. (New) The method of claim 23, wherein the third gene is derived from an environmental library.

29. (New) The method of claim 27 or 28, wherein the environmental library is derived from

30. (New) The method of claim 29, wherein uncultured microorganisms comprise a mixture of terrestrial microorganisms, a mixture of marine microorganisms, or a mixture of terrestrial and marine microorganisms.

31. (New) The method of claim 29, wherein the uncultured microorganisms are extremophiles.

32. (New) The method of claim 31, wherein the extremophiles are selected from the group consisting of thermophiles, hyperthermophiles, psychrophiles, and psychrotrophs.

33. (New) The method of claim 27 or 28, wherein the library is created by obtaining an environmental sample, enriching the environmental sample for prokaryotic organisms and selecting against eukaryotic organisms, isolating nucleic acids from the enriched sample, fractionating the nucleic acids, and cloning the isolated nucleic acids into a vector.

34. (New) The method of claim 33, wherein the nucleic acids are amplified prior to cloning into the vector.

35. (New) The method of claim 33, wherein the vector is an expression vector.

36. (New) A method for detecting the ability of a molecule to affect the interaction between a first and second protein, comprising:

(i) contacting a first hybrid protein with a second hybrid protein in the presence of the test molecule, the first hybrid protein comprising:

(a) a first domain and the first protein; and

the second hybrid protein comprising:

(b) a second domain and the second protein;

wherein association of the first and second hybrid proteins in the absence of the test molecule results in the absence or presence of a detectable response; and

(ii) comparing the detectable response in the presence of the test molecule with the detectable response in the absence of the test molecule.

37. (New) The method of claim 36, wherein the detectable response is the expression or repression of a detectable gene.

38. (New) The method of claim 37, further comprising, prior to (i):

(A) providing a prokaryotic host cell containing the detectable gene; and

(B) providing a first gene capable of being expressed in the host cell, the first gene encoding the first hybrid protein.

39. (New) The method of claim 38, further comprising, prior to (i):

(C) providing a second gene capable of being expressed in the host cell, the second gene encoding the second hybrid protein.

encoding the test molecule

41. (New) The method of claim 40, further comprising, prior to (i):

(E) introducing said first, second and third genes into the host cell; and

(F) allowing expression of the genes.

42. (New) The method of claim 41, wherein the first domain is a DNA binding domain and the second domain is a transcriptional activation domain.

43. (New) The method of claim 41, wherein the first and second domains form a transcriptional repressor.

44. (New) The method of claim 41, wherein the third gene is derived from an environmental library.

45. (New) The method of claim 44, further comprising, prior to (i):

(G) obtaining an environmental sample; and

(H) enriching the sample for prokaryotic organisms and selecting against eukaryotic organisms.

46. (New) The method of claim 45, further comprising producing a normalized library, comprising, prior to (i):

(I) isolating nucleic acids from said enriched environmental sample;

(J) fractionating the isolated nucleic acids;

(K) melting the recovered fractions and allowing subsequent reannealing; and

(L) amplifying any single-stranded nucleic acids present in the sample.